The Pharmacokinetics of BPA

Similarities in Human and Animal Metabolism Suggest Higher Exposure than Thought

Bisphenol A (BPA) has been shown to cause adverse health effects in animals, but attempts to extrapolate human health effects from this evidence are impeded by unanswered questions about routes and levels of exposure, metabolism, and whether animal models are appropriate proxies for humans. New findings show the kinetics of BPA metabolism are very similar in humans, monkeys, and mice and also suggest greater human exposure than previously estimated [***EHP* 119(4):422–430; Taylor et al.**].

BPA in food and beverage packaging likely underlies most human oral exposure, and dermal and inhalation exposure may occur from other sources. BPA has been assumed to undergo rapid metabolism (conjugation) and clearance from the body. However, recent human biomonitoring data showed serum concentrations of unconjugated BPA, the bioactive form, at levels much higher than predicted given earlier assumptions about the amount of BPA ingested by humans and its expected rate of clearance.

The authors of the current study studied clearance of radiolabeled unconjugated BPA in rhesus macaques and CD-1 mice, then compared the results with those from a previous oral dosing study in women. In the first experiment, female monkeys received deuterated BPA (dBPA) at 400 μg per kg body weight once a day for a week. Blood samples were collected prior to dosing and several times on days 1 and 7. The second experiment involved an oral dose of 400 μg ^{3}H-BPA per kg body weight to female CD-1 mice and measurements of the unconjugated compound in serum over the next 24 hours. A second group of mice received a single dose of varying amounts of ^{3}H-BPA, with unconjugated serum levels measured 24 hours later, and a third group received a single dose of BPA at 100,000 μg/kg, with serum assessed for unconjugated BPA several times over the next 24 hours.

Unconjugated dBPA concentrations in monkeys averaged 0.5 ng/mL over 24 hours and peaked at 3.94 ng/mL 1 hour after treatment. These values are comparable to medians of 0.3–4.0 ng/mL reported in human biomonitoring studies. The amount of BPA needed to achieve the serum concentrations in monkeys far exceeded the 2007 U.S. Food and Drug Administration human exposure estimate of 0.16 μg/kg/day as well as the U.S. Environmental Protection Agency's daily intake dose of 50 μg/kg. Results from the mouse experiments showed a linear relationship between BPA dose and unconjugated BPA in serum, with the kinetics of metabolism remarkably similar to those observed in monkeys and humans.

If the reported plasma BPA concentrations in humans are accurate, the results suggest human exposure is currently underestimated and that there may be significant sources of exposure though non-oral routes. Additionally, they support CD-1 mouse studies as being relevant for estimating serum levels of unconjugated BPA in humans.

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Where There Is Asbestos, There Is Mesothelioma

Filling in the Data Blanks

Malignant mesothelioma is caused almost exclusively by exposure to asbestos, and countries that have used asbestos nearly always have cases of mesothelioma. Tracking the disease has proved difficult, however, because not all developing countries that use asbestos collect mesothelioma incidence data. In a new global estimate of unreported mesothelioma, researchers predict that at least one case of disease goes unreported for every four to five known cases worldwide [***EHP* 119(4):514–518; Park et al.**].

The authors compared cumulative asbestos use from the U.S. Geological Study with disease cases reported to the World Health Organization. Because symptoms of mesothelioma often appear decades after exposure, the authors examined the relationship between the 15-year cumulative number of reported mesothelioma cases during 1994–2008 and cumulative asbestos use during 1920–1970 among countries with data on both mesothelioma and asbestos use. The resulting relationship helped them predict the number of unreported mesothelioma cases in countries providing information on asbestos use but not on mesothelioma.

The authors found that cumulative asbestos use in 89 countries totaled more than 65 million metric tons during 1920–1970. Of the 56 countries also reporting mesothelioma data, there were more than 174,000 estimated cases and 92,000 reported deaths during 1994–2008 (most mesothelioma patients succumb to the disease shortly after diagnosis, so numbers of new cases are very similar to numbers of deaths from the disease). When extrapolating these data to the 33 countries not reporting mesothelioma, the authors estimated an additional 39,000 cases would have occurred during that same 15-year period.

This estimate is conservative, say the authors, and they warn that because asbestos has a long industrial life span, and its use has quintupled since 1970, many countries should anticipate a higher disease burden in the years to come. The new study does not account for this 40-year increase.

The authors propose that developed countries share their experience and technology to help developing countries better diagnose, report, and manage cases of mesothelioma. They also argue that all countries should move toward a complete ban on asbestos—although the long latency period means mesothelioma deaths would continue for decades, the disease would eventually disappear as asbestos use is phased out and exposure is eventually eliminated.

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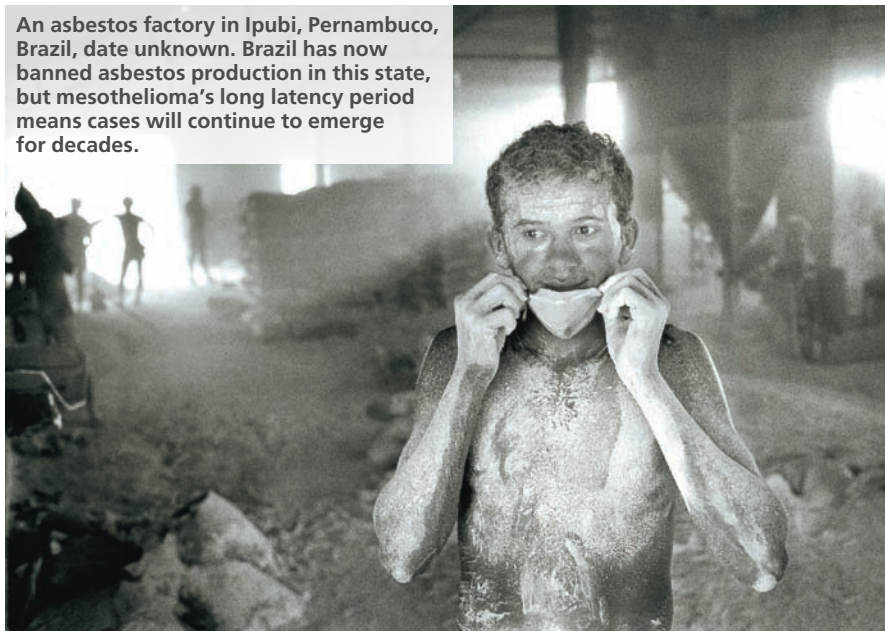

An asbestos factory in Ipubi, Pernambuco, Brazil, date unknown. Brazil has now banned asbestos production in this state, but mesothelioma's long latency period means cases will continue to emerge for decades.

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